## REMARKS

The Office Action mailed June 28, 2002 has been received and carefully reviewed. Claims 1-5, 12, 14, and 15 having been amended, the pending claims are claims 1-15. Of these, the claims presently under examination are claims 1-3 and 12-15.

Claim 1 is amended to recite structural and functional features of the claimed polypeptide. Amendment to claim 1 is supported by the specification at, for example, page 9, lines 14-17; page 11, line 32 through page 12, line 5; page 12, lines 11-15; and page 12, lines 15-18.

The Examiner is requested to note that the elected amino acid sequence of PPSS-II" (SEQ ID NO:15; Fig. 3) includes, as subunits, the following amino acid sequences: SEQ ID NO:16 (proprotein; specification at page 6, lines 18-19); SEQ ID NO:17 (N-terminal extension "pre" sequence; page 6, line 30, bridging to page 7, line 2; Fig 3); SEQ ID NO:18 (N-terminal extension "pro" sequence; page 6, lines 25-26) and SEQ ID NO:19 (putative N-terminal signal sequence; page 6, lines 12-13). Together, SEQ ID NO:17 (the "pre" sequence) and SEQ ID NO:16 (proprotein) make up PPSS-II" (SEQ ID NO:15). The proprotein sequence (SEQ ID NO:16) is made up of the SEQ ID NO:18 (the "pro" sequence) and the [$Tyr^7$,$Gly^{10}$]SS14 peptide sequence (SEQ ID NO:2).

## Elections/Restrictions

As noted by the Examiner, Applicants elected the invention of Group I (claims 1-3 and 12-15), with traverse, and further elected amino acid sequence SEQ ID NO:15 as the species for prosecution on the merits. Applicants acknowledge with appreciation that amino acid sequence SEQ ID NO: 18 (11 amino acids), a subunit of SEQ ID NO:15 (111 amino acids), was searched in addition to amino acid sequence SEQ ID NO:15.

In response to the claim objections indicated at paragraph 14 of the Office Action mailed June 28, 2002, generic claims 1-3 and 12-15 are amended to delete recitation of non-elected SEQ

ID NO:3 and other amino acid sequences such that the claims now recite the elected species, SEQ ID NO:15 and/or subsequences thereof (e.g., SEQ ID NOs:16, 17, 18 and 19). However, Applicant disagrees with the necessity of amending a generic claim in view of a species election, and reserves the right to reverse this amendment and request that the generic claims examined upon an indication that claims directed to the elected species are allowable, in accordance with MPEP 809.02.

## Priority

Applicants wish to correct the record by noting that the filing date of the priority application, U.S. Provisional Application 60/168,934 was December 3, 1999, not December 1,1999. The Filing Receipt and PAIR data correctly reflect the actual filing date of December 3, 1999.

## Objection to the Disclosure

The Examiner objected to the inclusion in the specification of a browser-executable hyperlink. The specification is amended to render these citations non-executable.

## Rejection under 35 U.S.C. §101

The Examiner rejected claims 1-3 under 35 U.S.C. §101, because the claimed invention is directed to non-statutory subject matter, a somatostatin polypeptide or bioactive analog or subunit thereof. Claim 1 is amended to recite an "isolated or purified" somatostatin polypeptide or bioactive analog or subunit thereof, as suggested by the Examiner. Reconsideration and withdrawal of the rejection of claims 1-3 under 35 U.S.C. §101 is requested.

## Rejection under 35 U.S.C. §112, First Paragraph

The Examiner rejected claims 1, 12, and 13 under 35 U.S.C. §112, first paragraph, because the specification, while being enabling for polypeptides or fusion proteins comprising SEQ ID NOs: 15, 16 and 18, does not reasonably provide enablement for any other somatostatin

polypeptides or fusion proteins comprising a portion of SEQ ID NO:15. In particular, the Examiner states that other than SEQ ID NO:15 and its major fragments set forth in SEQ ID NOs:16 and 18, the disclosure fails to provide sufficient guidance and information regarding the structural and functional requirements commensurate in scope with what is encompassed by the instant claims. This rejection is respectfully traversed.

Claim 1 is amended to recite structural and functional features of the claimed polypeptide. In particular, amended claim 1 recites:

> 1. An isolated or purified somatostatin polypeptide comprising a polypeptide selected from the group consisting of:
>
> (a) a polypeptide comprising SEQ ID NO:15;
>
> (b) a subunit of the polypeptide of (a) comprising SEQ ID NO:16 and at least 7 contiguous amino acids from SEQ ID NO:17;
>
> (c) an analog of the polypeptide of (a) that has an amino acid sequence at least about 85% identical to SEQ ID NO:15; and
>
> (d) an analog of the subunit of (b) having an amino acid sequence at least about 90% identical to the amino acid sequence of the subunit;
>
> wherein the somatostatin polypeptide binds to a somatostatin receptor.

Claim 12 is amended to depend from claim 1.

Claim 1, as amended, recites as a component of the Markush group a polypeptide *subunit* that comprises SEQ ID NO:16 and at least 7 contiguous amino acids from SEQ ID NO:17, thereby providing structural characterization of the subunit. A polypeptide *analog* (or subunit thereof) is *structurally defined* as having 85% sequence identity to SEQ ID NO:15 (90% in the case of the subunit). The claimed polypeptide is *functionally defined* as binding to a somatostatin receptor. An assay for readily assessing whether a candidate somatostatin polypeptide binds to a somatostatin receptor is taught in Example V at page 38, line 28 bridging

to page 39, line 19, of the specification. It is respectfully submitted that the specification enables the use of the claimed invention commensurate in scope with the claims, as amended.

The Examiner states that the specification does not teach *which portions* of SEQ ID NO:15 are critical to the activity of the polypeptide, nor does it teach *which modifications* will result in protein mutants with the same function as the protein of SEQ ID NO:15. To the extent that this criticism still applies to the claims as amended, Applicants disagree. It is not necessary to be able to predict *exactly which sequences* having 85% (or 90%) identity to SEQ ID NO:15 (or subunit thereof) will retain bioactivity, because candidate sequences can be easily screened for somatostatin receptor binding using the binding assay described in the specification.

The Federal Circuit has approved of the use of screening methods to enable the production of subject matter that could not be predicted *a fortiori* to be a member of the claimed genus. In *In re Wands*, 8 U.S.P.Q.2d, 1400, Fed. Cir. 1988) (cited by the Examiner) the court considered whether undue experimentation was required to practice and invention directed to methods for immunoassay of HbsAg using monoclonal antibodies. Specifically, the issue was whether undue experimentation was required to produce the high-affinity IgM monoclonal antibodies used in the claimed assay, in view of experimental data that was not in dispute. *In re Wands* at 1401. It was agreed that the starting materials were publicly available and the methods used to prepare hybridomas and to screen them for high-affinity IgM antibodies against HbsAg were either well known to the monoclonal antibody art or adequately disclosed. *In re Wands* at 1404. The Board agreed with the Examiner that undue experimentation was nonetheless required in order to practice the invention, citing the low success rate in obtaining hybridomas that produced the desired monoclonal antibodies. Specifically the Board found that only 4 out of 143 hybridomas tested fell within the claims, and that, further, that the antibodies that proved to be high-affinity IgM came from only 2 of 10 experiments. The Board thus determined that Appellant's methods were not predictable or reproducible, and concluded that the low rate of demonstrated success showed that a person skilled in the art would have to engage in undue experimentation to make antibodies that fell within the claims. *In re Wands* at 1404-1405.

The court viewed the data differently and suggested that the success rate in obtaining useful hybridomas was actually substantially better than that determined by the Board. *In re Wands* at 1406. More important, however, is the court's acknowledgment of the nature of the field of the invention and its impact on the issue of what constituted undue experimentation within the field. The court specifically recognized that monoclonal antibody technology involves screening hybridomas to determine which ones secrete the antibody with the desired characteristics, and that practitioners of that art are prepared to eliminate many negative hybridomas in order to find one that makes the desired antibody. *In re Wands* at 1406. The court further recognized that in the monoclonal antibody art, an "experiment" was viewed not simply as the screening of a single hybridoma, but is rather an entire attempt to make a monoclonal antibody against a particular antigen. The applicant showed this procedure was carried out three times, each time resulting in at least one antibody that satisfied all of the claim limitations. The court concluded that the amount of effort needed to obtain such antibodies was not excessive. *In re Wands* at 1407.

Using the legal analysis employed in *In re Wands*, it is clearly not necessary for an art worker in the field of molecular genetics or biochemistry to be able to predict *in advance* which members of a group of candidate compounds or compositions will fall within the claimed class, as long as sufficient guidance exists to enable the art worker to screen the group and identify members of the claimed class. It is well-settled that a considerable amount of experimentation is permissible if it is merely routine, or if the specification provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. *Ex parte Jackson*, 217 U.S.P.Q. 804, 807 (1982). In biotechnology, the use of screening methods to identify and select particular molecules of interest from a heterogenous population created by random laboratory procedures or procedures having a low level of specificity or a low success rate is standard practice, and art workers are highly skilled in the use and evaluation of such screening procedures. What is required under *In re Wands* is sufficient guidance to identify and select the biological molecules that satisfy the limitations of the claims, using screening procedures available to the art or disclosed in the specification.

The Examiner's attention is directed to the specification at page 9, lines 23-28, describing examples of conservative amino acid changes that can be expected to be made to a somatostatin polypeptide without altering activity. It is well known in the art of protein biochemistry that polypeptides can tolerate conservative mutations at numerous sites without the elimination of protein activity, and these conservative mutations are well understood and characterized. To make additional somatostatin polypeptides, others will do exactly what is taught in the present specification: start with the disclosed sequence (e.g., Applicants' SEQ ID NO:15), "tweak it" at locations that are not likely to disrupt activity, and test the new sequence for receptor binding activity. The application thus fully teaches how to make the class of polypeptides claimed in claims 1, 12 and 13, as amended.

Reconsideration and withdrawal of the rejection of claims 1, 12 and 13 under 35 U.S.C. §112, first paragraph, is respectfully requested.

Rejection under 35 U.S.C. §102(b)

The Examiner rejected claims 1 and 2 under 35 U.S.C. §102(b) as being anticipated by Moore et al. (*General and Comparative Endocrinology, 98*:253-261 (1995)), stating that Moore et al. teaches a preprosomatostatin II which is a bioactive analog of SEQ ID NO:15 and shares 79.7 % sequence identity with SEQ ID NO:15. This rejection is respectfully traversed.

Claim 1, as amended, recites a somatostatin polypeptide comprising an analog of a polypeptide comprising SEQ ID NO:15 that has an amino acid sequence at least about 85% identical to SEQ ID NO:15. As the percentage identity recited in the claim is 85% but the sequence identity between SEQ ID NO:15 and the prior art polypeptide is only 79.7 %, it is respectfully submitted that the rejection is overcome. Reconsideration and withdrawal of the rejection under 35 U.S.C. §102(b) is respectfully requested.

Rejection under 35 U.S.C. §103(a)

The Examiner rejected claims 12 and 13 under 35 U.S.C. §103(a) as being unpatentable over Moore et al. (*General and Comparative Endocrinology, 98*:253-261 (1995)),

as applied to claims 1 and 12, in view of Hobart et al. (EU 46669 A1, March 3, 1982). In view of the amendment to claims 1 reciting 85% identity as discussed in response to the rejection under 35 U.S.C. §102(b) and further in view of the amendment of claim 12 to depend from claim 1, Applicant submits that the rejection is overcome. Reconsideration and withdrawal of the rejection under 35 U.S.C. §103(a) is respectfully requested

**Summary**

It is respectfully submitted that the pending claims 1-3 and 12-15 are in condition for allowance and notification to that effect is respectfully requested. The Examiner is invited to contact Applicants' Representatives, at the below-listed telephone number, if it is believed that prosecution of this application may be assisted thereby.

Respectfully submitted for
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The undersigned hereby certifies that this paper is being transmitted by facsimile in accordance with 37 CFR §1.6(d) to the Patent and Trademark Office, addressed to Assistant Commissioner for Patents, Washington, D.C. 20231, on this 28th day of **OCTOBER, 2002**, at 6:08 pm (Central Time).

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